

Hematuria

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Urine Analysis and Microscopy

- Can be POC or in the Lab (Point of Care)
- In the Lab: two step test
- First: Dipstick
- Second: Microscopy
 - Spin (Centrifuge) ----> Sediment + Supernatant
 - Observe the **Sediment** under Microscope

Objectives

- Understand definitions: Macroscopic and Microscopic Hematuria
- Learn to rule out non-Hematuric red urine
- Glomerular vs. Non-Glomerular Hematuria
- When to reassure a patient and when to follow up
- When to consult Urology

Dipstick			
POC	Urine Appearance Urine Dipstick	Dark yellow	
	Specific Gravity Urine Dipstick	1.020	
	Bilirubin Urine Dipstick	Negative	
	pH Urine Dipstick	6	
	Urobilinogen Urine Dipstick	0.2 mg/dl	
	Blood Urine Dipstick	Large	
	Glucose Urine Dipstick	Negative	
	Ketones Urine Dipstick	Negative	
	Protein Urine Dipstick	1+ (30 mg/dl)	
	Nitrite Urine Dipstick	Negative	
	Leukocytes Urine Dipstick	Negative	
			Dipstick
			LAB

Hematuria

- Macroscopic Hematuria (Gross)
- Microscopic Hematuria
- Glomerular vs. Non-Glomerular Hematuria
- Transient Hematuria
- Historical Clues
- Take Home Message

Gross Hematuria

- Urine discoloration: red or brown urine
- Color does not necessarily reflect the degree of blood loss: Patient's and Staff Panic
- Intermittent excretion of red to brown urine seen in a variety of clinical conditions other than bleeding into the urinary tract (later)
- Passage of clots: lower urinary tract source

Red Urine with True Gross Hematuria

- The initial step: Centrifugation of the specimen
- Sediment vs. Supernatant
- Red to Brown Sediment with clear Supernatant ---> True Hematuria
- Exception RBC lysis in Urine (diluted urine etc..)

“False” Gross Hematuria

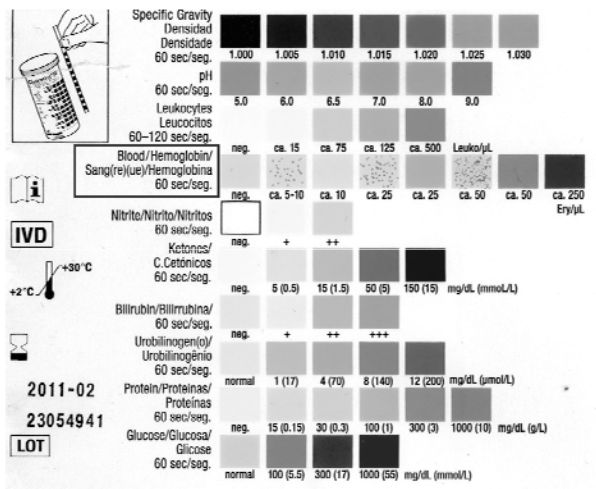
- Possibility of blood contamination e.g. menstruating and post-partum women: Repeat when cause ceases
- Options: Direct catheterization; Tampon etc.
- Factitious

Red Urine without Hematuria

- Red to Brown Supernatant ---> Check for Heme
- Heme: Heterocyclic compound with Iron at the center

Red Urine without Hematuria

- Red to Brown Supernatant ---> Check for Heme
 - Heme: Heterocyclic compound with Iron at the center
 - Hemoglobin and Myoglobin have pseudo peroxidase activity: Catalyzes the reaction
- $H_2O_2 + \text{Chromogen} \rightarrow \text{Oxidised chromogen (coloured)} + H_2O$

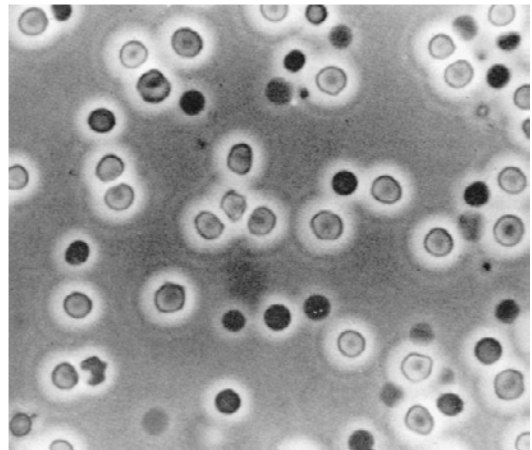


Red Urine without Hematuria

- Red to Brown Supernatant ---> Check for Heme
(Heme = Myoglobin or Hemoglobin)
- Supernatant Heme +ve ---> Myoglobin or Hemoglobin
- Supernatant Heme -ve ---> porphyria; use of bladder analgesic phenazopyridine; ingestion of beets شمندر.....

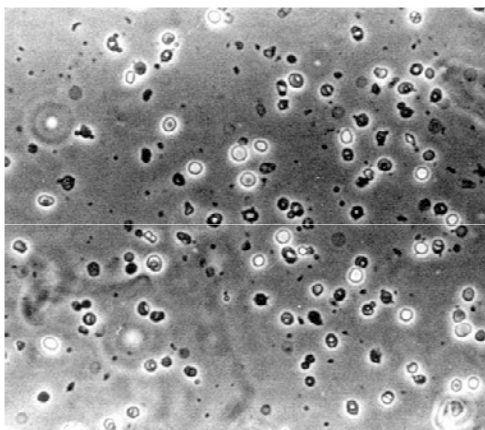
Microscopic Hematuria

- Often discovered by accident on dipstick
- Abnormal Hematuria: Three or more RBCs per high power field by Microscopy
- Positive dipstick -----> Always confirm by Microscopy
- False positive dipstick: Semen, Alkaline Urine and Myoglobinuria
- False negative dipstick: Ingestion of large amount of Vitamin C



Glomerular Hematuria

- Immune-mediated injury to the glomerular capillary wall: Glomerulonephritis
- Noninflammatory glomerulopathies
e.g. Thin basement membrane nephropathy (localized gaps in the glomerular capillary wall)

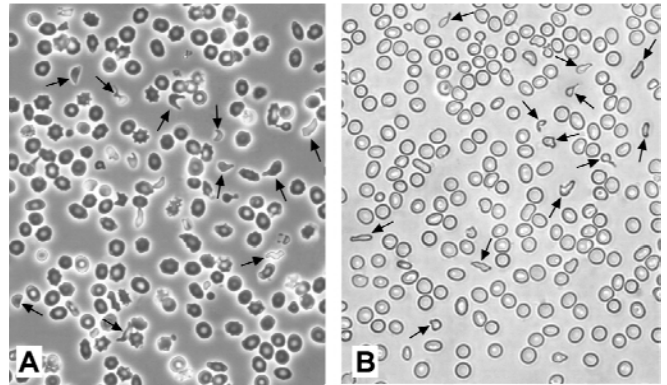
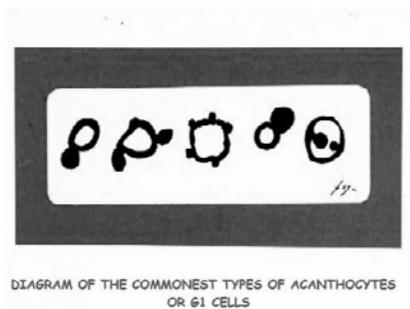


Glomerular Hematuria RBC Morphology

- Red cell morphology is essential
- Extrarenal bleeding: Typically uniform and round (as in a peripheral blood smear) with
- Dysmorphic appearance with renal lesions, particularly in glomerular diseases

Glomerular Hematuria RBC Morphology

- Segmental Loss of Membrane, resulting in marked variability in red cell shape and a reduction in mean red cell size
- Anisocytosis: RBCs of unequal size
- Poikilocyte: Abnormally shaped cell
- Acanthocytes: Dysmorphic erythrocytes with vesicle-like protrusions
- Crenated RBCs: RBC with projections extending from a smaller central area, like a spiked ball



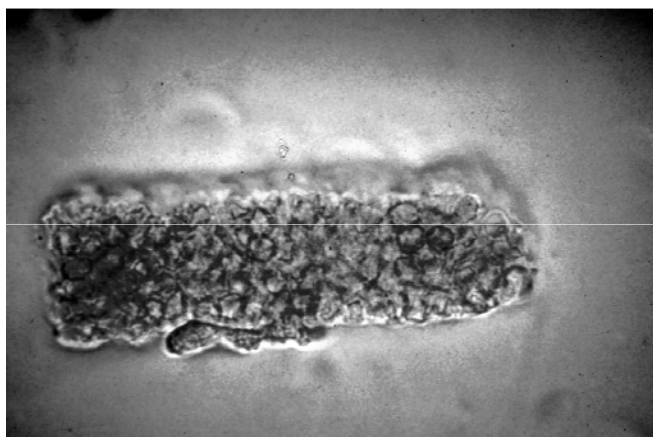
(A) Isomorphic (crenated and non-crenated) urinary erythrocytes intermingled with erythrocytes of irregular size and shape, most of which are indicated by the arrows (phase contrast microscopy, original magnification 400x).
(B) Unstained peripheral blood film showing anisocytes and poikilocytes identical to those seen in the urine (arrows) (bright field microscopy, original magnification 400x).

Casts

- Urinary Casts: Cylindrical structures produced by the kidney and present in the urine in certain disease states
- Formed distal convoluted tubule and collecting ducts of Nephrons
- Dislodge and pass into the urine
- Detected by microscopy
- They form via precipitation of Tamm-Horsfall mucoprotein which is secreted by renal tubule cells

Glomerular Hematuria

- Red Cell Casts -----> Diagnostic of glomerulonephritis or vasculitis
- No Red Cell Casts -----> Cannot exclude glomerular disease



Glomerular Hematuria

Tips

- Blood clots, if present, are almost always due to extraglomerular bleeding
- Proteinuria that is temporally related to the hematuria is suggestive of glomerular disease
- **However**, a large amount of gross bleeding can cause abnormal proteinuria

Distinguishing extraglomerular from glomerular hematuria

	Extraglomerular	Glomerular
Color (if macroscopic)	Red or pink	Red, smoky brown, or "Coca-Cola"
Clots	May be present	Absent
Proteinuria	<500 mg/day	May be >500 mg/day
RBC morphology	Normal	Some RBCs are dysmorphic
RBC casts	Absent	May be present

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Transient Hematuria

- Young patients with transient Hematuria: No etiology found in a significant proportion
- Fever, infection, trauma, and exercise are potential causes of transient hematuria
- Transient Hematuria + Pyuria + Bacteriuria +/- Dysuria = UTI
- **However**, transient Hematuria in patients above 40 year: Investigate for possible malignancy

Historical Tips

- Recent URTI ----> ? Postinfectious glomerulonephritis or IgA nephropathy or sometimes hereditary nephritis
- +ve family history of renal disease, as in hereditary nephritis, PKD, sickle cell disease
- Unilateral flank pain, +/- radiation to groin ----> ? Ureteral obstruction (stone vs. malignancy)

Historical Tips

- Vigorous exercise/trauma in the absence of another possible cause
- Anticoagulation alone does not explain hematuria
- Menstrual blood... always repeat if +ve

Further Tips

- Travel ----> Schistosoma haematobium or tuberculosis
- Sterile pyuria + hematuria ----> ? Renal TB, analgesic nephropathy, Interstitial diseases

So....

- Consult Urology if:
- If non-glomerular hematuria
 - If UTI treated, and persistent Hematuria
 - If above 40 without obvious cause
 - If suspecting malignancy
 - If stone or obstruction suspected

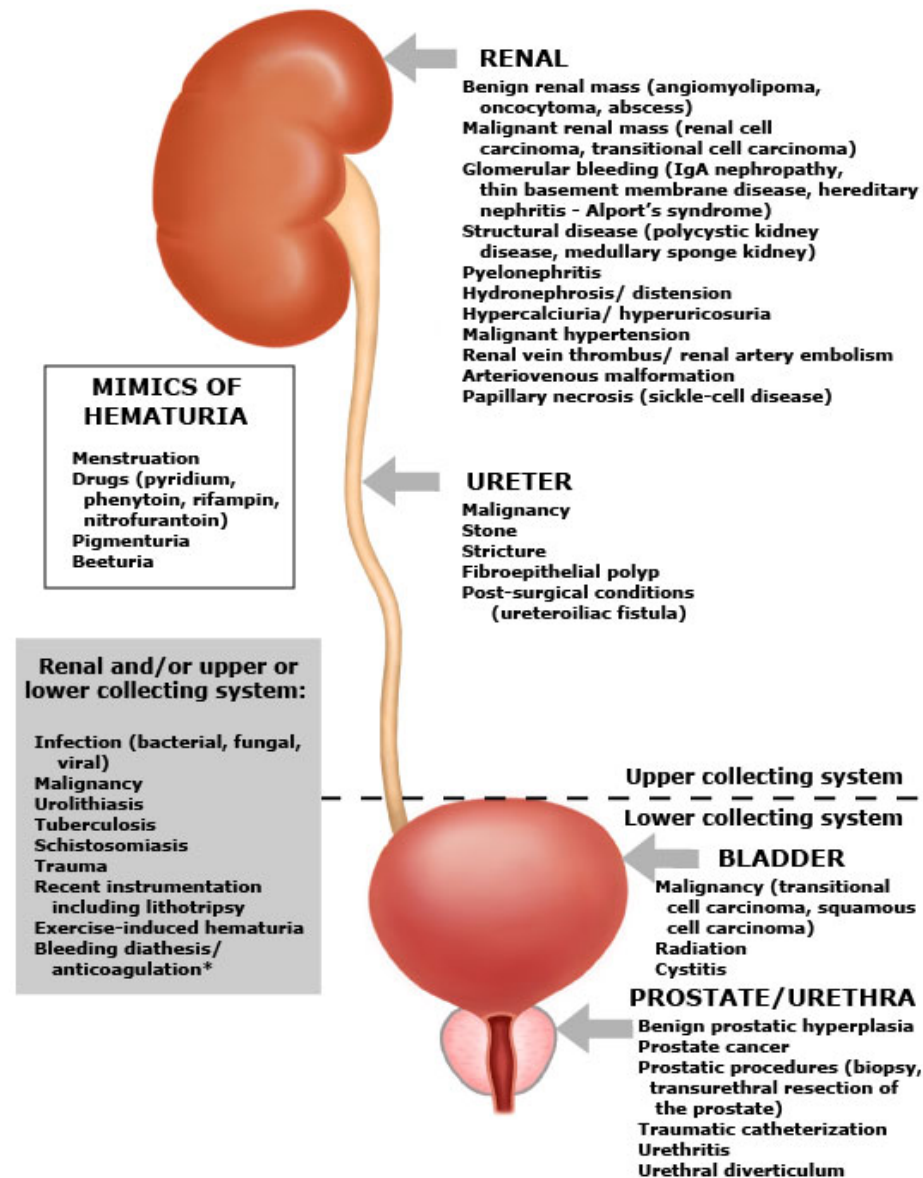
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Consider further Nephro work up if:

- Evidence of Glomerular disease: History, Casts, RBC morphology, Renal Failure
- Proteinuria
- Renal Failure
- Persistent

Thank You

Causes of hematuria



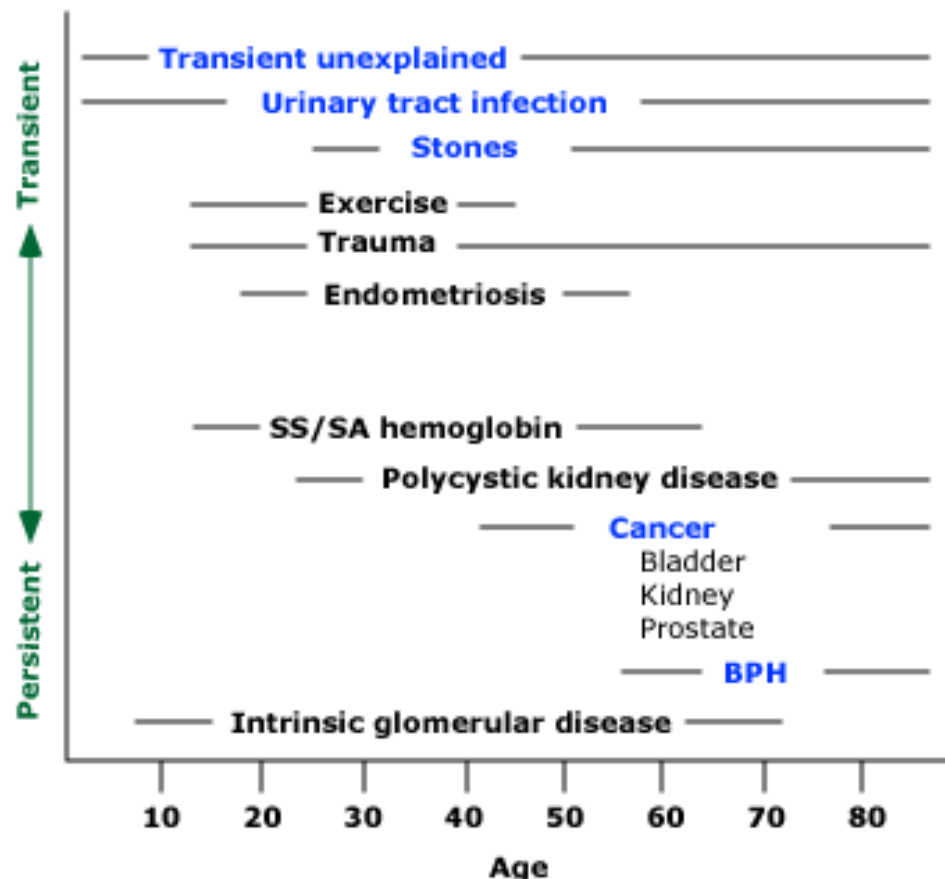
* Hematuria may not be attributed solely to alterations in coagulation or platelet function until competing causes have been ruled out.

Courtesy of Michael Kurtz, MD.

Causes of heme-negative red urine

Medications
Doxorubicin
Chloroquine
Deferoxamine
Ibuprofen
Iron sorbitol
Nitrofurantoin
Phenazopyridine
Phenolphthalein
Rifampin
Food dyes
Beets (in selected patients)
Blackberries
Food coloring
Metabolites
Bile pigments
Homogentisic acid
Melanin
Methemoglobin
Porphyrin
Tyrosinosis
Urates

Major causes of hematuria by age and duration



Schematic representation of the major causes of hematuria in relation to the age at which they usually occur (horizontal axis), transience or persistence (vertical axis), and frequency (blue implies more frequent).

BPH: benign prostatic hyperplasia.